

CLAIMS

What is claimed is:

- 5 1. A method of classifying a brain tumor comprising the steps of:
a) obtaining a sample of cells derived from a brain tumor;
b) isolating a gene expression product from at least one informative gene
from one or more cells in said sample; and
c) determining a gene expression profile of at least one informative gene,
wherein the gene expression profile is correlated with a specific brain tumor sub-
type.
- 10 2. The method of Claim 1, wherein the brain tumor type is selected from the group
consisting of: medulloblastoma, rhabdoid tumor, primitive neuroectodermal
tumor, pineoblastoma and glioblastoma.
- 15 3. The method of Claim 2, wherein the brain tumor type is a medulloblastoma or a
glioblastoma.
M&C/S
- 15 4. The method of Claim 3, wherein the medulloblastoma sub-type is classic
medulloblastoma or desmoplastic medulloblastoma.
5. The method of Claim 2, wherein the expression profile comprises expression of
Zic or NSCL-1.
- 20 6. The method of Claim 1, wherein the expression profile comprises expression of
TrkC.
- 20 7. The method of Claim 1, wherein the gene expression product is mRNA.
M&C/S

8. The method of Claim 7, wherein the gene expression profile is determined utilizing specific hybridization probes.

Mw Cls 9
The method of Claim 7, wherein the gene expression profile is determined utilizing oligonucleotide microarrays.

- 5 10. The method of Claim 1, ~~wherein the gene expression product is a polypeptide.~~

11. The method of Claim 10, wherein the gene expression profile is determined utilizing antibodies.

- Subh 10*
12. A method according to Claim 1, wherein one or more informative genes is selected from the group consisting of the genes in Figures 2A-2B, 3A-3B, 5A-5B and 6B-6C.

- GvB 11*
13. A method according to Claim 1, wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1B.

- B 2 12*
14. A method of predicting the efficacy of treating a brain tumor comprising the steps of:

- a) obtaining a sample of cells derived from a brain tumor;
b) isolating a gene expression product from at least one informative gene from one or more cells in said sample; and
c) determining a gene expression profile of at least one informative gene, wherein the gene expression profile is correlated with a treatment outcome, thereby classifying the sample with respect to treatment outcome.

20

15. The method of Claim 14, wherein the brain tumor type is selected from the group consisting of: medulloblastoma, rhabdoid tumor, primitive neuroectodermal tumors, pineoblastoma and glioblastoma.
16. The method of Claim 15, wherein the brain tumor type is a medulloblastoma or
5 a glioblastoma.
17. The method of Claim 16, wherein the medulloblastoma sub-type is classic medulloblastoma or desmoplastic medulloblastoma.
18. A method according to Claim 14, wherein the gene expression product is mRNA.
- 10 19. A method according to Claim 18, wherein the gene expression profile is determined utilizing specific hybridization probes.
20. A method according to Claim 18, wherein the gene expression profile is determined utilizing oligonucleotide microarrays.
- 15 21. A method according to Claim 14, wherein the gene expression product is a polypeptide.
22. A method according to Claim 21, wherein the gene expression profile is determined utilizing antibodies.
23. A method according to Claim 14, wherein the predicted treatment outcome is survival after treatment.

Sub A2

24. A method according to Claim 14, wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1B.

25. A method according to Claim 14, wherein one or more informative genes is selected from the group consisting of the genes in Figures 2A-2B, 3A-3B, 5A-5B and 6B-6C.

5 26. A method of assigning a brain tumor sample to a treatment outcome class, comprising the steps of:

- 10 a) determining a weighted vote for one of the classes of one or more informative genes in said sample in accordance with a model built with a weighted voting scheme, wherein the magnitude of each vote depends on the expression level of the gene in said sample and on the degree of correlation of the gene's expression with class distinction; and
- b) summing the votes to determine the winning class,
- 15 wherein the winning class is the treatment outcome class to which the brain tumor sample is assigned.

Mb CJS

27. The method of Claim 26, wherein the weighted voting scheme is:

$$V_g = a_g (x_g - b_g),$$

20 wherein V_g is the weighted vote of the gene, g ; a_g is the correlation between gene expression values and class distinction; $b_g = (\mu_1(g) + \mu_2(g))/2$ is the average of the mean \log_{10} expression value in a first class and a second class; x_g is the \log_{10} gene expression value in the sample to be tested; and wherein a positive V value indicates a vote for the first class, and a negative V value indicates a vote for the second class.

- A3

28. The method according to Claim 26, wherein the informative genes are selected from the group consisting of the genes in Figures 1A-1B.

29. The method according to Claim 26, wherein the informative genes are selected from the group consisting of the genes in Figures 2A-2B, 3A-3B, 5A-5B and 6B-6C.

5 30. An oligonucleotide microarray having immobilized thereon a plurality of oligonucleotide probes specific for one or more informative genes selected from the group consisting of the genes in Figures 1A-1B, 2A-2B, 3A-3B, 5A-5B and 6B-6C.

10 31. A method for evaluating drug candidates for their effectiveness in treating brain tumors comprising:
 - obtaining samples of cells derived from a brain tumor;
 - isolating a gene expression product from at least one informative gene from one or more cells in said samples; and
 - determining a gene expression profile of at least one informative gene, wherein the gene expression profile is correlated with the effectiveness of the drug candidate in treating brain tumors.

15 32. A method for monitoring the efficacy of a brain tumor treatment comprising:
 - obtaining samples of cells at various time points derived from a patient being treated;
 - determining the expression profile of the samples;
 - classifying the samples for treatment outcome based on the expression profile; and
 - comparing the treatment outcome class of the samples at various times during treatment,

20

25

wherein the efficacy of brain tumor treatment is determined.

33. A method for predicting tumorigenesis comprising:

- a) obtaining samples of cells at various time points derived from a patient;
- b) determining the expression profile of the samples;
- 5 c) classifying the samples as tumorigenic or non-tumorigenic based on the expression profile; and
- d) comparing the tumorigenic class of the samples at various times,

such that the onset of tumorigenesis can be predicted.

and
B4